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SYNTHESIS AND CYCLOADDITIONS OF A BICYCLOBUTANE BRIDGED DIAZOKETONE

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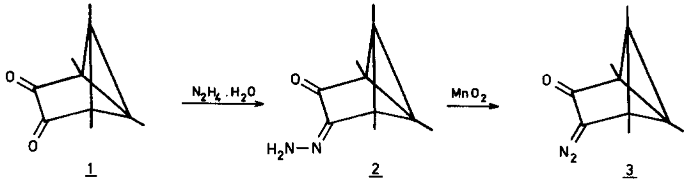
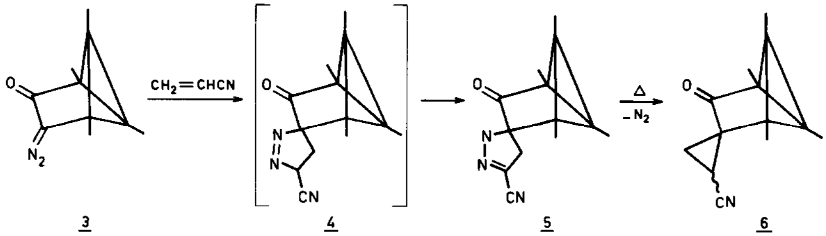
Diazoketones are widely used as precursors in the preparation of various kinds of ring-systems by reaction with unsaturated substrates[1]. The reaction of diazoketones with electron-poor alkenes yields pyrazolines[1]; or, in case of preliminary loss of nitrogen, the corresponding keto-carbenes add to alkenes to yield either cyclopropanes or dihydrofurans[2,3]. Within the context of our interest in the chemistry of bicyclobutane-bridged functionalities[4-6], we prepared diazoketone 3 and investigated whether the various cycloaddition reactions would afford products still containing an intact highly strained bicyclobutane moiety or products in which (valence) isomerization has occurred. A number of representative reactions is reported herewith. Diazoketone 3 was prepared by refluxing the readily available diketone 1[6] (164 mg, 1 mmol) with $N_2H_4.H_2O$ (0.05 ml, 1mmol) in methanol solution (10 ml) for 1.5 hours; after removal of the methanol, crude hydrazone 2[7a] (180 mg) was dissolved in dichloromethane (15 ml), dried over Na_2SO_4 and treated with MnO_2[8] (0.6 g, 0.7 mmol) with stirring for 4 hours. The slurry was filtered over celite, leaving after evaporation of the solvent an orange oil (170 mg), crude diazoketone 3[7b], which was used in the cycloaddition experiments without further purification[9].

SCHEME 1

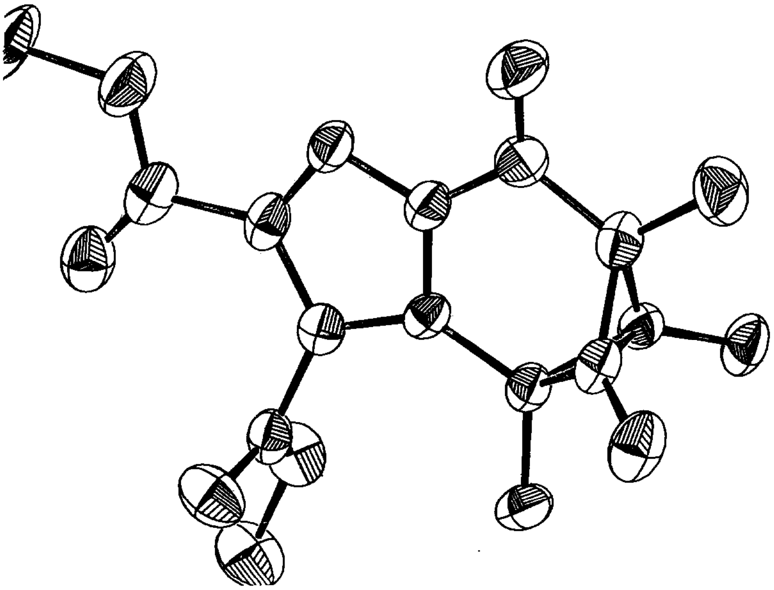


Treatment of a dichloromethane solution of 3 (prepared from 1 mmol of 1) with excess acrylonitrile (1 ml) at reflux temperature for 15 minutes gave 2-pyrazoline 5[7c] as a yellow oil in 70% yield. The formation of 2-pyrazoline 5 probably occurs *via* intermediacy of 1-pyrazoline 4, which is the initial product of the 1,3-dipolar cycloaddition. Preliminary results indicate that on thermolysis (xylene, 130^{0}C, 24 hours), 5 loses nitrogen to afford a mixture of isomeric cyano-substituted cyclopropane derivatives 6.

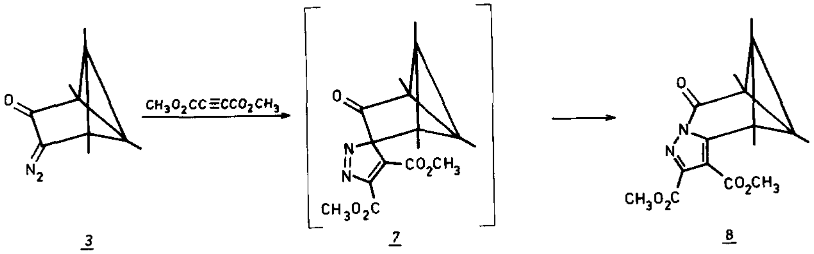
SCHEME 2



The reactivity of 3 towards electron-poor alkynes is exemplified by the cycloaddition of dimethyl acetylenedicarboxylate (1 equivalent) in dichloromethane (room temperature, 16 hours), which afforded pyrazole 8^{7d} as a brown viscous oil (yield 60%, based on 1 taken); repeated crystallization from CCl_4 yielded pure 8 (m.p. 140.5-141.3^{0}C), the structure of which was recently proven by X-ray techniques which is shown below[12]. Indications for the intermediacy of pyrazolenine 7 have not been obtained; however, it is known that rapid [1,5]-sigmatropic acyl-migrations of the type 7 → 8 do occur in pyrazolenines[13].

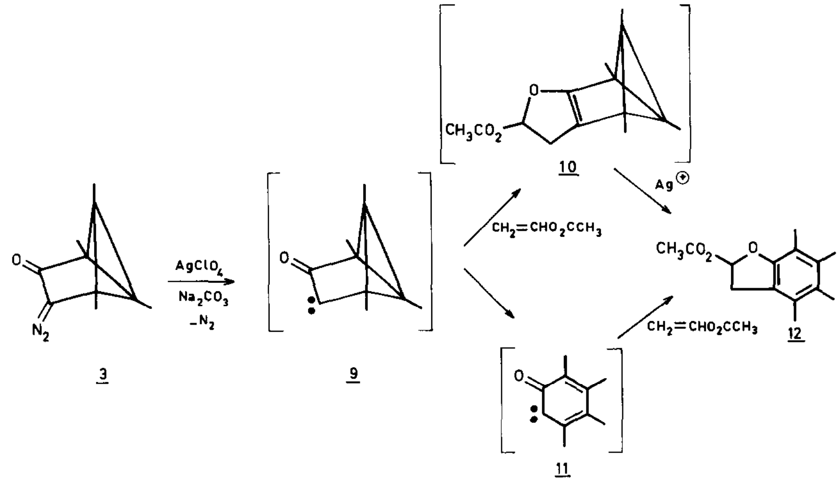


SCHEME 3



In contrast to the above-mentioned reactions of 3 with electron-poor dipolarophiles, no reaction was observed when 3 was treated at room temperature with the electron-rich alkene vinyl acetate. However, when a vinyl acetate solution (2 ml) of 3 (prepared from 1 mmol of 1) was added at -70°C to a slurry of $AgClO_4$ (0.1 mmol) and Na_2CO_3 (1 mmol) in vinyl acetate, followed by warming to room temperature and work-up, compound 12 was obtained (yield 34%, based on 1 taken); m.p. 108.4-109.5°C (hexane, methanol). A possible mechanism for this reaction is shown in Scheme 4. The first step probably involves an $Ag^{\oplus}$-catalyzed loss of nitrogen from 3, leading to intermediate (free or complexed) carbene 9. In the next step carbene 9 may undergo a 1,3-dipolar addition to vinyl acetate affording benzvalene-ether 10, followed by an $Ag^{\oplus}$-catalyzed valence isomerization[4] to yield dihydrobenzfuran 12. Alternatively, carbene 9 may rearrange to carbene 11 that also can yield compound 12 by a 1,3-dipolar cycloaddition to vinyl acetate. Preliminary results show that treatment of 3 in the presence of $Ag^{\oplus}$ with other electron-rich alkenes such as isobutene and tetramethylethene results in the same mode of reaction.

SCHEME 4



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7) a. Hydrazone 2. MS: m/e found 178.111, calc. 178.113 ($M^{\oplus}$); IR: 3420 (NH), 1700 (C=O), 1600 (C=N) cm^{-1}; PMR ($CDCl_3$): δ 1.14 (s, 3H), 1.23 (s, 3H), 1.59 (s, 6H), 7.18 (broad, 2H); CMR ($CDCl_3$): δ 2.9, 3.5, 5.6, 33.4, 40.5, 50.6, 144.9, 196.2 ppm.

   b. Diazoketone 3[10]. MS: m/e found 148.089, calc. 148.090 ($M^{\oplus}-N_2$); IR: 2060 (N=N), 1690 (C=O) cm^{-1}; PMR ($CDCl_3$): δ 1.03 (s, 3H), 1.32 (s, 3H), 1.47 (s, 6H); CMR ($CDCl_3$): δ 2.8, 4.8, 7.3, 25.8, 37.2, 37.4, 51.2, 196.6 ppm.

   c. 2-Pyrazoline 5. MS: m/e found 229.126, calc. 229.122 ($M^{\oplus}$); IR: 3290 (NH), 2210 (C≡N), 1720 (C=O), 1525 (C=N) cm^{-1}; PMR ($CDCl_3$): δ 1.09 (s, 3H), 1.12 (s, 3H), 1.48 (s, 3H), 1.52 (s, 3H), 2.76-2.92 (AB-system, J = 17 Hz, 2H), 6.85 (broad, 1H); CMR ($CDCl_3$): δ 2.3, 2.8, 4.2, 5.3, 24.0, 26.8, 37.9 (t, J_{CH} = 138 Hz), 42.8, 51.9, 73.1, 114.3, 119.5, 210.5 ppm.

   d. Pyrazole 8[11]. MS: m/e 318 ($M^{\oplus}$); IR: 1730 (C=O), 1570 (C=N) cm^{-1}; PMR ($CDCl_3$): δ 1.36 (s, 3H), 1.42 (s, 3H), 1.60 (s, 6H), 3.90 (s, 6H); CMR ($CDCl_3$): δ 4.2, 9.1, 10.9, 38.8, 44.0, 46.9, 51.9, 52.1, 114.6, 144.0, 147.8, 160.9, 163.3, 167.5 ppm;
   Analysis: Calcd. for $C_{16}H_{18}O_5N_2$: C 60.37, H 5.70, N 8.80; Found: C 60.08, 59.97, H 5.65, 5.61, N 8.93, 8.88.

   e. Dihydrobenzfuran 12. MS: m/e 234 ($M^{\oplus}$); IR: 1730 (C=O) cm^{-1}; PMR ($CDCl_3$): δ 2.09 (s, 3H), 2.21 (s, 12H), 3.0-3.7 (m, 2H), 6.82 (dd, J_1 = 3 Hz, J_2 = 6 Hz, 1H) ppm. Double irradiation at δ 6.82 ppm resulted in an AB-system at δ 3.08 and 3.38 ppm (J_{AB} = 17 Hz).
   Analysis: Calcd. for $C_{14}H_{18}O_3$: C 71.76, H 7.74; Found: C 71.34, 71.11; H 7.74, 7.58.
8) MnO_2 prepared according to Attenburrow *et al.*, *J. Chem. Soc.*, 1952, 1094.
9) Diazoketone 3, with an average purity of about 70%, is thermally unstable above 10°C. (Attempts to purify 3 by preparative TLC and HPLC resulted in decomposition.) Stored in solution at -20°C, 3 is fairly stable for several days.
10) Compare for CMR-data of diazoketones: T.A. Albright and W.J. Freeman, *Org. Magn. Res.*, 9, 75 (1977).
11) Compare for CMR-data of pyrazoles: H. Dürr, H. Kober, R. Sergio and V. Formacek, *Chem. Ber.*, 107, 2037 (1974).
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